

IN THE SPECIFICATION

Please replace the title with the following new title:

Automated In-Process Ratio Mass Spectrometry

Please replace the paragraph beginning on page 1, line 9 with the following replacement paragraph:

This invention relates to a method and apparatus for an in-process, automated analysis using a ratio measurement. More specifically, the disclosed In-process, Atmospheric Pressure Interface, Mass Spectrometer (IP-API-MS) apparatus and related method uses a ratio measurement to characterize the amounts or concentrations of analytes. This characterization is an elemental and speciation threshold measurement method that is may be optimized for quality assurance at and near instrumental detection limits. The threshold measurement method is automated and may be employed for unattended operation of an In-process, Atmospheric Pressure Interface, Mass Spectrometer (IP-API-MS). The IP-API-MS apparatus is designed for identification and quantification of elemental contaminants or compounds and species in fluids.

Please replace the paragraph beginning on page 1, line 19 with the following replacement paragraph:

~~It has been known to employ mass~~ Mass spectrometry instrumentation ~~in measuring parts-per-billion (ppb)~~ is frequently used as the technique of choice in measuring parts-per-billion (ppb) ppb and sub-ppb levels of elements or compounds in aqueous and other solutions as well as in gases. Mass spectrometers are typically operated and regularly calibrated by experienced technicians. In many cases, however, unattended operation of the mass spectrometer is desired. These cases may include remote operation, around the clock

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monitoring, or operation either in hostile environments, or where human interaction must be minimized. One such case is that of contamination monitoring and control in the wet process baths, such as, for example, the semiconductor industry which requires a clean room environment where minimal human interaction is desired. Installation of real time, in-situ, sensors into clean room process is a major defect reduction challenge in the industry. International Technology Roadmap for semiconductors 1999 Edition: Defect Reduction, Sematech, Austin Tex., (pg. 270) (1999).

Please replace the paragraph beginning on page 2, line 20 with the following replacement paragraph:

Viscosity differences between the sample and standard matrices may also cause unequal instrument responses associated with changing sample introduction rates which are inevitable in real world situations. Matrix effects altering solution viscosity or ionization efficiency can result in calibration changes such as shown in Figure 1 (curve C). ~~The present invention uses modification of IDMS in order to achieve measurements that are optimized for quality assurance at and near instrumental detection limits without the need for traditional calibration.~~

Please replace the paragraph beginning on page 9, line 2 with the following replacement paragraph:

The present invention employs a ratio measurement analogous to that used in modifications of traditional IDMS methods that enhance and improve measurement at and near the detection limit of mass spectrometers. The ratio measurement allows the characterization of a sample. To obtain the ratio measurement, a spike is added to a sample. After equilibration, the spiked sample is ionized using atmospheric pressure ionization and the

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resulting ions introduced into a mass spectrometer to form a ratio. A processor may then use the ratio to characterize the sample. These modifications provided for quality assurance of both ultra-trace elemental and speciated measurements.

Please replace the paragraph beginning on page 9, line 6 with the following replacement paragraph:

The method and apparatus of this invention employs the relatively-mild ionization provided by an atmospheric pressure ionization process such as, for example, electrospray in contrast to the relatively-harsh ionization encountered within is preferably to be used with an IP-API-MS instrument instead of an ICP-MS. Because of this relatively-mild ionization process, species information such as the concentration of a particular ionization state of an element or molecular complex within a sample is preserved thereby eliminating the necessity of a physical separation step after equilibration of the spike and sample. In contrast, such species information may be lost as a species is ionized in an ICP-MS process. Neither HPLC nor ICP-MS is an essential instrumentation in the IP-API-MS apparatus. In the present method, no chromatographic separation is required. The equilibrium between spike and sample species is achieved by dynamical pretreatment, which may be complex, oxidation, or other, of both sample and spike to transform them to the same species before pre-concentration and determination.

Please replace the paragraph beginning on page 9, line 13 with the following replacement paragraph:

In the present invention, an analyte may be characterized in a sample without requiring the provision of an isotopically-enriched spike in the same speciated form as the analyte. Instead, the analyte and spike may be transformed to the same species during

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equilibration of the spike and sample, through, for example, dynamical pre-treatment such as oxidation or simply through a reaction of the spike with the sample's matrix. the labeled species (frequently multiple species simultaneously) are being created in solution and are not previously determined in composition and structure until evaluated for structural information. Quantification is of the elemental ion and speciation information first established in process through dynamic equilibrium established with a non-complexing salt of an enriched stable isotope in real time and in process. The methods provide dynamic labeling and duality of mass spectrometer. Additionally, simultaneous species may be evaluated without separation in one embodiment and sequentially in another. The dynamics and sequences are very different from known methods.

Please replace the paragraph beginning on page 9, line 22 with the following replacement paragraph:

In one embodiment, the present invention relates to a method and apparatus that Unlike traditional IDMS this method enhances and improves measurement at and near the detection limit of mass spectrometers. In this embodiment, the spike concentration is adjusted based upon pre-determined criteria such as an expected concentration range for the analyte to enhance characterization of an analyte using a ratio measurement. An apparatus has been developed to use the method for in-process measurement, using an Atmospheric Pressure Interface coupled to a Mass Spectrometer (IP-API-MS). The IP-API-MS apparatus is designed for identification and quantification of elemental contaminants or compounds and species in fluids without reliance upon the high temperature argon plasma for equilibrium or requiring a HPLC separation step prior to measurement.

Please delete the paragraph beginning on page 10, line 1.

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Please replace the paragraph beginning on page 10, line 11 with the following replacement paragraph:

In one embodiment of the invention, the method and apparatus enables the IP-MS to be operated in an unattended manner that is a substantial departure from attended operation protocol where operator calibration and analysis are typically performed. Direct comparison against a calibration curve is unnecessary through the use of ratio measurements. This is a departure from traditional instrument operation where concentrations of elements are made in comparison and where instrument drift requires frequent re-calibration required for quantitation. In one embodiment, the ratio of the analyte to the spike in a spiked sample is optimized for accuracy and quality assurance at and near the detection limits of the measurement.

Please delete the paragraph beginning on page 10, line 20.

Please delete the paragraph beginning on page 11, line 22.

Please delete the paragraphs beginning on page 12, line 7 through page 13, line 12.

Please delete the paragraph beginning on page 14, line 9.

Please replace the paragraph beginning on page 16, line 3 with the following replacement paragraph:

Referring now in greater detail to Figure 2, a preferred method of the present invention will be considered. For convenience of disclosure, although reference will be made to

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monitoring of wet baths of the type used in clean rooms for wafer production in the semiconductor industry, it will be appreciated that the method is not so limited. The present method has the capability of performing both qualitative and quantitative analysis regarding specie and elemental contamination levels at the ultra-trace level and at the quantitative detection limit of the instrument. Traditionally, a plurality of baths, each containing aqueous or organic solvent solutions, are provided with the wafers to be cleaned being sequentially taken from one bath to the next. As a result, it becomes important to determine whether contaminants in each bath are within tolerable limits. The failure to do so can result in very expensive and time-consuming loss of product. The present invention contemplates either sequential analysis of each bath or simultaneous analysis of samples from two or more baths. It also provides a means for ascertaining on the basis of identification of the particular specie or element which specific bath is subject to contamination if contamination exists. One may also determine the origin of a contaminant based on its species composition, the component of the baths and the chemical reactions occurring therein.

Please replace the paragraph beginning on page 18, line 18 with the following replacement paragraph:

If it is desired to determine, qualitatively, the presence of a specie, the sample from sample introduction is introduced into the chemical modification step 12, wherein information provided from sample analysis 6 to microprocessor 10 will have entered data collection and analysis 14, which, in turn, distributes the information 16 which is passed onto controller 20, which, in turn, provides an output signal along lead 24 to chemical modification 12 to provide whatever adjustment in the chemistry, such as pH or reagent content, or physical properties, such as temperature, to the sample prior to the next stage of sample processing. The sample, as modified, is then delivered to the solution-handling unit which if the objective is

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qualitative, evaluation of the sample will deliver the same to atmospheric pressure ionization unit 32 which, in a preferred form, is an electrospray ionizer. This unit serves to ionize the components of the solution including the elements and species and, if desired, de-solvates the sample. The output of this unit is delivered to mass spectrometer 36, which may preferably be a time of flight mass spectrometer, or quadrapole mass spectrometer. The information from the mass spectrometer is delivered to the microprocessor 10 into the data collection and analysis unit 14, which, in turn, delivers it for information distribution to unit 16. Information which is to be employed in controlling operation of the instrument will be fed back to a sample introduction 2, spike introduction 38, chemical modification 12, solution handling 26, atmospheric pressure ionization 32, and mass spectrometer 36 for appropriate action. Further, to the extent to which the information may involve a departure from a desired concentration of contaminants, if an early warning is to be provided or an alert or shutdown ordered, the information is also delivered to the system interface 40 which controls the operation of the physical system which is being monitored by the instrument. This information may also be provided to operational personnel who would be provided with not only the warning and alert information, but also data regarding the then current readings, long-term trends, and other information of interest, including optimization information. Considering another mode of operation of the method, if it is desired to obtain quantitative determinations of an element, the sample introduction 2 delivers a sample to the spike introduction location, wherein enriched separated isotopes are mixed in dilute or a weakly complexing mode where they are mixed with the sample and subjected to equilibration. The equilibrated sample is then passed through chemical modification 12 and solution handling 26 from which it goes to liquid chromatograph 48 and then to atmospheric pressure ionization 32, after which, it is subjected to speciation processing ~~50~~ 56 from which it passes to mass spectrometer 36 with the output of the mass spectrometer being processed in microprocessor 10 and, as appropriate, passed on

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to controller 12 and/or system interface 40. For the elemental mode, the voltage ranges from about 200 to 1,000 volts and preferably about 350-400 volts and for the specie mode from about 2-30 volts. In this approach, an enriched isotope is provided in the spike introduction 38 for each specie or element of contaminant sought to be monitored. If the sample were a gas sample, it would pass from solution handling 26 to gas chromatograph 56 and follow the process.

Please replace the paragraph beginning on page 22, line 5 with the following replacement paragraph:

Figure 6 shows the ratio and de-convoluted result for Ag measured by ID API (ES)-MS. A 1 ppm Ag in 1% HNO₃ was spiked with Ag-109 quantitatively. Five replicate measurements were performed under the same instrument conditions. The counts of isotope ¹⁰⁷Ag-107 and ¹⁰⁹Ag-109 were extracted and the ratio of ¹⁰⁹/¹⁰⁷ Ag-109/Ag-107 was calculated. The measured ratio of ¹⁰⁹/¹⁰⁷ Ag-109/Ag-107 was 1.2303 ± 0.016 (1.3% variance which shows as the top line in the figure). The sample concentration was de-convoluted based on the measured ratio, and final result was 0.904 ± 0.05 ppm (5.5% variance, which shows as bottom line in the Figure). By comparison with Figure 4 which shows an approximate 25% variance there is a significant improvement in precision over the test period of 15 min. in this case. This demonstrates the ability of the invention to improve the precision of the measurement for ES-MS.

Please replace the paragraph beginning on page 28, line 1 with the following replacement paragraph:

In Figure 10, the demonstration of threshold measurement for 0.01 ppb Ni below instrument quantitative detection limit is shown. The standard deviation of instrument signal

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is equal to the square root of the signal. The uncertainty of traditional measurement is expressed as 3 times of standard deviation of such measurement. Monte Carlo simulation is used to demonstrate the establishment of threshold using the novel method. 200 sets of normally distributed numbers having a mean value of 0 and a standard deviation of 1 are applied to the simulation for each spike. The ratio of sample volume to spike volume is 1:1. The uncertainties of de-convoluted concentrations are expressed as 90% confident level of 200 simulations for each spike.

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